REMARKS

The present application contains claims 1-88, the status of which is as follows:

(a) Claims 1-44, 57, 59-65, and 82-88 have been canceled without prejudice.

(b) Claim 46-52, 54-56, 58, 68-69, and 71-81 were previously presented.

(c) Claims 45, 53, 66, 67, and 70 have been currently amended.

Amendments to the claims

Claims 45 and 66 have been amended to recite that moving erythrocytes are optically imaged at first and second points in the subject's cardiac cycle, and that roughness on the inner wall of a blood vessel is identified by comparing flow characteristics of the erythrocytes within the blood vessel at the respective points in the cardiac cycle. These amendments find support in the following paragraph of the specification:

> [0070] Furthermore, **perturbation of the blood pressure, for example by the use of drugs or exercise, can provide two sets of measurements. A comparison of the value of the derived parameters or characteristics from these two sets, may be used to obtain an index for the roughness of the blood vessels**, such as for instance, if the amount of local turbulence, which can be quantified by standard fluid-dynamic tools or by results obtained from a model, is significantly different at the two pressures.
>
> [0071] Such perturbation also exists naturally as a result of the heartbeat of the subject, the blood pressure changing cyclically during each heartbeat. According to a further preferred embodiment of the present invention, the imaging of the optically accessible blood vessel is synchronized to predetermined points in time of the heartbeat when the blood pressure is known to be different, and **the flow characteristics at these two points in time are compared to obtain an index for the roughness of the blood vessels**.

Claims 53, 67 and 70 have been amended to conform with the amendments to claims 45 and 66.

Response to claim rejections under 35 U.S.C. 103(a)

The Examiner rejected independent claims 45 and 66 under 35 U.S.C. 103(a) over WO 99/63882 to Grinvald, in view of "Retinal microvascular abnormalities and incident stroke: the atherosclerosis risk in communities studies," (Wong, October 2001), further in view of US 5,727,561 to Owsley. Claims 45 and 66 have been amended to recite that moving erythrocytes are optically imaged **at first and second points in the subject's cardiac cycle**, and that roughness on the inner wall of a blood vessel is identified by comparing flow characteristics of the erythrocytes within the blood vessel at the respective points in the cardiac cycle. The Applicant respectfully submits that none of the aforementioned references recites or renders obvious identifying roughness on the inner wall of a blood vessel based on optically imaging erythrocytes at first and second points in the subject's cardiac cycle, and comparing the flow characteristics of the blood vessel at the respective points in the cardiac cycle. In this regard, it is noted that in the present Office Action, the Examiner stated the following with respect to the aforementioned references:

> Further, they do not disclose that their method includes the limitations of instant claims 56 and 58, which disclose that the first blood pressure corresponds to a first point in a cardiac cycle of the subject wherein said second blood pressure corresponds to a second point in the cardiac cycle of the subject, and wherein the optical imaging steps comprise optically imaging moving erythrocytes within said at least one optically accessible blood vessel when the subject's cardiac cycle is respectively at said first and second points in the subject's cardiac cycle

[Page 7, first paragraph of the Office Action]

Claims 46-53, being dependent from claim 45, and therefore of narrower scope than claim 45, are also allowable over the references cited by the Examiner. Claims 67-81, being dependent from claim 66, and therefore of narrower scope than claim 66, are also allowable over the references cited by the Examiner.

Independent claim 54 was rejected under 35 U.S.C. 103(a) over WO 99/63882 to Grinvald, in view of "Retinal microvascular abnormalities and incident stroke: the atherosclerosis risk in communities studies," (Wong, October 2001), further in view of

US 5,727,561 to Owsley, still further in view of "In vivo quantification of blood flow and wall shear stress in the human abdominal aorta during lower limb exercise" (Taylor, March 2002).

Claim 54 recites that moving erythrocytes are imaged at first and second blood pressures and that a roughness index of an inner wall of a blood vessel is determined by utilizing differences in respective flow characteristics of the erythrocytes at the first and second blood pressures.

The Examiner cited the second and third paragraphs of page 403, right column of Taylor, which state the following:

> Scans were performed at rest and during steady-state exercise conditions (150% of resting heart rate) within the range of light exercise (35%–59% of maxHR).[24] In order to maintain this level of exercise, the subjects monitored their own heart rate (heart rate was displayed in real-time on the pulse monitor) and adjusted pedaling speed as necessary to maintain a constant heart rate.
>
> Cine PC-MRI techniques were used to measure through-plane blood flow velocity as a function of position at the supraceliac, suprarenal, and infrarenal levels at rest and during exercise as shown in Fig. 2.[23] The image acquisitions were gated to the cardiac cycle using a plethysmograph, and data was retrospectively reconstructed at 16 discrete time points within the cardiac cycle irrespective of *RR* interval. Patients breathed nor-

The above paragraphs describe a technique in which blood flow velocity was determined at respective points in subjects' cardiac cycles, both during rest and exercise. It is not obvious in view of the technique described in Taylor to **determine a roughness index of an inner wall of a blood vessel by determining flow characteristics of erythrocytes within the blood vessel at respective blood pressures** (e.g., at respective points in the cardiac cycle, or at rest and during exercise), **and utilizing differences between the flow characteristics**, as recited in claim 54.

The technique recited in claim 54 is described in the following paragraphs of the present application:

> [0070] Furthermore, perturbation of the blood pressure, for example by the use of drugs or exercise, can provide two sets of measurements. **A comparison of the value of the derived parameters or characteristics from these two sets, may be used to obtain an index for the roughness of the blood vessel**s, such as for instance, if the amount of local turbulence, which can be quantified by standard fluid-dynamic tools or by results obtained from a model, is significantly different at the two pressures.
>
> [0071] Such perturbation also exists naturally as a result of the heartbeat of the subject, the blood pressure changing cyclically during each heartbeat. According to a further preferred embodiment of the present invention, the imaging of the optically accessible blood vessel is synchronized to predetermined points in time of the heartbeat when the blood pressure is known to be different, and **the flow characteristics at these two points in time are compared to obtain an index for the roughness of the blood vessels.**

The technique recited in claim 54, which is described in the above-quoted paragraphs, is for determining a roughness index of blood vessels by utilizing differences between flow characteristics at respective blood pressures. According to this technique, the movement of the erythrocytes at the respective blood pressures is analyzed in order to determine a characteristic (the roughness index) of the blood vessel wall. This is not obvious in view of Taylor, which describes the measurement of blood flow velocity at respective blood pressures, but does not describe the derivation of a roughness index of the blood vessel wall, on the basis of these measurements. In general, none of the references cited by the Examiner describes the derivation of roughness of the blood vessel wall by utilizing differences between the flow characteristics within the blood vessel at respective blood pressures, as recited in the claimed invention. Therefore, the Applicant respectfully submits that claim 54 is allowable over the references cited by the Examiner. Claims 55, 56, and 58, being dependent from claim 54, and therefore of narrower scope than claim 54, are also allowable over the references cited by the Examiner.

It is noted that the arguments provided hereinabove for the allowability of claim 54 over Taylor, are equally applicable to independent claims 45 and 66, as currently amended.

The Applicant believes the amendments and remarks presented hereinabove to be fully responsive to all of the grounds of rejection and objection raised by the Examiner. In view of these amendments and remarks, the Applicant respectfully submits that all of the claims in the present application are now in order for allowance. Notice to this effect is respectfully requested.

Respectfully submitted,

CLIFFORD J. MASS
LADAS & PARRY LLP
1040 AVENUE OF THE AMERICAS
NEW YORK, NEW YORK 10018-3738
REG.NO. 30086 (212) 708-1890